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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER

BALASUBRAMANIAN, VENKATARAMAN

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1624

DATE MAILED: 11/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/050,768 | KUO, SHEN-CHUN | |
| | Examiner | Art Unit | |
| | Venkataraman Balasubramanian | 1624 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 September 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>3</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' response, which included amendment to claims 4,6-7, 9-10, 15, 21-22, and 24, filed on 9/11/2002, is made of record.

Claims 1-28 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim.

1. Claim 1 is indefinite as it recites "a time sufficient enough to produce a compound of formula IA". As recites it is vague and unclear as to what is the sufficient time. This rejection is same as made in the previous office action. Applicants' argument to overcome this rejection is not persuasive. Applicants are claiming a process and as asserted by the applicants, if one trained in the art know all the parameters of the process, it would raise an issue what is the limitation that is not obvious. Furthermore, it also raises the issue whether reaction time to be treated as a limitation of the claim. In addition, a product may appear in any time form few seconds to minute hours etc. and it is not clear whether applicants is claiming the reaction should be stopped at that stage or to allowed to go to completion. Hence this rejection is maintained.

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2. Claim 1 is also vague and unclear as to the term "iodide". While the claim recites "in the presence of an iodide" which should be soluble in inert medium, the oxidizing/cyclizing agent also includes iodide as seen in page 8 of specification and it is not clear whether the latter iodide is excluded or included in the solubility requirement.
3. Recitation of "inert medium" in claim 1, renders the claim indefinite as there is no definition of this term in the specification. It is not clear what is included or excluded. The term as recited can even include inert gas atmosphere such as nitrogen or argon conventionally used and citing "inert medium" as a limitation would be misleading.
4. Claim 3 is indefinite as to the definition of Z which is recited as (H, Hal). It is not clear what is intended. Again applicants' argument is misplaced. It is not the definition of "H" or "Hal" that is questioned but the whole representation (H, Hal). Applicants have not addressed the issue and this rejection is also maintained.
5. Recitation of "a reagent that oxidizes NH_2 to NZ " in claim 3 is indefinite as one trained in the art would know which amino group is being referred to. Note there are three amino groups in compound of formula II but there is no teaching as to which one is being referred to.
6. Claims 10, 16 and 25 are deemed as indefinite as it is not clear what is included or excluded in the X and Y definition. In one hand claim recites X as leaving group as in claim 10, while in other claims it is a leaving group of the type that activates adjacent carbonyl group. It is not clear what X is. Furthermore, there is

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no definition of what is meant by a leaving that activates an adjacent carbonyl group. Claim 28 is also rejected herein as in this claim $X = -N(CH_3)-NH_2$ which is by no means can be treated as leaving group.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Bu_4I/H_5IO_6 as oxidizing/cyclizing agent, does not reasonably provide enablement for any or all oxidizing/cyclizing agent generically embraced in the claim language. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The following apply:

In evaluating the enablement question, following factors are considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1. The nature of the invention and the state of the prior art:

The invention is drawn to a process of making tetrazinone compound of generic formula IA wherein the compound of formula II is treated with an oxidizing/cyclizing agent to obtain compound of formula IA. Specification is not adequately enabled as

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to how to make these compounds with an oxidizing/cyclizing agent other than $\text{Bu}_4\text{I}/\text{H}_5\text{IO}_6$. Claim language as recited reads on any or all known oxidizing agent/cyclizing agent for which there is no corresponding enabling disclosure. Specification on page recites several agents which are known in literature as oxidizing agent but prior art search of these oxidizing agents do not teach them as oxidizing/cyclizing agents. Compound of formula II has more than one reactive site for oxidizing/cyclizing agent and can show propensity to react with the oxidizing agent. Besides the amino of the hydrazine group, there is an amino group in the imidazole ring, on the amide group, in addition to a double bond bearing nitrogen. There is no prior art which suggests that all these groups would be inert to any or all oxidizing agent generically embraced in the claim language. See Encyclopedia of reagents for Organic Synthesis under various oxidizing agents (not provided).

2. The predictability or lack thereof in the art:

Prior art search in the related area does not suggest how to make these compounds by using the hydrazine II as intermediate with variety of oxidizing agents. Hence the process as applied to the above-mentioned compounds using an oxidizing/cyclizing agent generically claimed by the applicant is not an art-recognized process and hence there should be adequate enabling disclosure in the specification with working example(s).

4. The amount of direction or guidance present:

Examples illustrated in the experimental section or written description offer no guidance or teachings as to how perform the process of making the said tetrazinones using different oxidizing/cyclizing agent.

5. The presence or absence of working examples:

Although there is a single example shown in the specification it is limited to $\text{Bu}_4\text{I}/\text{H}_5\text{IO}_6$ as an oxidizing/cyclizing agent. There are no representative examples of other oxidizing/cyclizing agent given the fact that there are more than one amino group and nitrogen atom in the compound of formula II., which may also undergo oxidation if not cyclization.

6. The breadth of the claim:

Specification has no support, as noted above, for use of any or all oxidizing/cyclizing agent generically embraced in the claim language that would lead to desired compound of formula I with said reactive amino groups and there is also no valid chemical reasoning for one trained in the art to expect that all these functional groups would be inert toward oxidizing/cyclizing reaction conditions. Note the prior art cited in the Information Disclosure Statement clearly shows reactivity of 5-amino group in the imidazole ring.

7. The quantity of experimentation needed:

The quantity of experimentation needed would be an undue burden on skilled art in the chemical art since there is inadequate guidance given to the skilled artisan for the many reasons stated above. Even with the undue burden of experimentation, there is no guarantee that one would get the product of desired

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structure, namely compound of formula I embraced in the instant claims in view of the prior art teachings.

Thus, factors such as "sufficient working examples", the "level of skill in the art and predictability, etc. have been demonstrated to be sufficiently lacking in the case for the instant claims.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Bu_4I as soluble iodide, does not reasonably provide enablement for any or all iodide generically embraced in the claim language. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The following apply:

The scope of the claim as recited includes any or all iodide for which there is no enabling disclosure. Applicants are asserting in the specification that the iodide functions as catalyst for the reaction and therefore the iodide is a critical limitation for the process. Without knowing what iodide is included or excluded, one need to extensive experimentation to arrive at a suitable iodide given the fact that solubility of iodide would also to be considered in the choice of the iodide. Prior art does not teach how to select an iodide suitable for the instant reaction scheme and the example recited in the specification is limited to Bu_4NI which is known to be soluble in organic solvent. Hence the specification is not adequately enabled to make the product of formula I with iodide other than Bu_4NI .

Claim 26 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for some X, does not reasonably provide enablement for X=OH embraced in the claim language. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The following apply:

Applicants are claiming a species, which is not enabled in the specification. Example shown does not enable one to make N-carboxylated compound claimed in the instant claim. Factors such as "sufficient working examples", the "level of skill in the art and predictability, etc. are sufficiently lacking and it would be undue experimentation to arrive at the desired product. Even then there is no guarantee that the product would be stable enough for further processing.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10-15, 25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al. J. Org. Chem. 62: 7288-7294, 1997.

Wang et al. teaches the compound of formula shown in claim 25. See page 7289, scheme 3, compound 14a, 14b, 14c. See page 7292, column 2 for the experimental details.

Claim 25 is rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al. J.Chem. Soc., Perkin Transactions I 10: 1669-1675, 1998.

See example 7 on page 1670. Note the compound meets the X definition.

Claim 25 is rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al. J.Chem. Soc., Perkin Transactions I 21: 2783-2787, 1995.

See example 5 on page 2783. Note the compound meets the X definition.

Claim 25 is rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al. J.Chem. Soc., Chemical Communications, 1687-1688, 1994.

See example 4 on page 1687. Note the compound meets the X definition.

Claim 25 is under 35 U.S.C. 102(b) as being anticipated by Wang et al. Chemical Communications, 4: 363-364, 1997.

See example 5 on page 363. Note the compound meets the X definition.

Claim 25 is under 35 U.S.C. 102(b) as being anticipated by Wang et al. Bioorg. Med. Chem., 692): 185-188, 1996.

See example 6 on page 186. Note the compound meets the X definition.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

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the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10, 23, 25 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chabala et al EP 0113,570 for reasons of record. To repeat:

Chabala et al. teaches several 5-amino-imidazole compounds for treatment of intestinal coccidiosis in animal, which include compounds claimed in the instant claims. herein. See page 2 formula shown therein and note the definition of various variable groups. Particularly note R¹ corresponds to instant group bearing X on the imidazole nitrogens. See pages 11- 28 for examples of compounds made

Instant claims differ from Chabala et al. in requiring specific protecting groups

However, Chabala et al. teaches the equivalency of exemplified R¹ groups in pages 11-28 with instantly claimed in the definition of R¹ groups recited in page 2. Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds variously substituted in the imidazole ring including various R¹ groups as permitted by the reference and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Applicants' argument to overcome this rejection is misplaced and not a proper factual analysis of 103(a) rejection.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Applicants' argument that once there is difference between the prior art and the claims at issue, then it precludes a prima facie obviousness is not tenable argument and is misinterpretation of the factual inquire process.

The item 2 states that one should the difference between the prior art and the instant claims and then address what is missing can be arrived by resolving the level of ordinary skill in the pertinent art.

In the instant case, reference Chabala et al. teaches the equivalency of exemplified R¹ groups in pages 11-28 with those claimed in the definition of R¹ groups recited in page 2. One trained in the art therefore would be motivated to make compounds bearing any or all R¹ permitted by the reference.

The rejection is proper and is maintained.

References cited in the Information Disclosure Statement (paper # 4) are made of record.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (703) 305-1674. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is Mukund Shah whose telephone number is (703) 308-4716.

The fax phone number for the organization where this application or proceeding is assigned (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.


Venkataraman Balasubramanian

11/22/2002